Defining radiotherapy target volumes using 18F-fluoro-deoxy-glucose positron emission tomography/computed tomography: still a Pandora's box?: in regard to Devic et al. (Int J Radiat Oncol Biol Phys 2010).

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DEFINING RADIOTHERAPY TARGET VOLUMES USING 18F-FLUORO-DEOXY-GLUCOSE POSITRON EMISSION TOMOGRAPHY / COMPUTED TOMOGRAPHY: STILL A PANDORA'S BOX?: In Regard to DEVIC *et al.* (*Int J Radiation Oncology Biol Phys* 2010 doi:10.1016/j.ijrobp.2010.02.015)

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To the Editor: Devic *et al.* (1) investigated the use of fixed thresholds to define NSCLC tumors PET volumes exhibiting heterogeneous uptake. They found no correlation between the CT-based and the PET-based volumes, and associated the observed variations with intrinsic properties of PET acquisition rather than their segmentation choice. They also concluded that PET-based volumes should not be used for radiotherapy dose painting/boosting. Several studies recently dealt with similar issues (2,3) by considering fixed threshold to determine tumor metabolic

volumes, demonstrating variability in the threshold values. Other recent studies demonstrated the limitations of fixed threshold and proposed more accurate and robust methods, from adaptive thresholding (4,5) to advanced algorithms (6-8) capable in some cases of handling heterogeneous uptake frequently characterizing tumors treated with radiotherapy.

Fixed thresholds cannot reliably define functional volumes due to their deterministic and binary nature whereas tumor uptake is variable, spatially heterogeneous and dependent on a large number of acquisition and reconstruction parameters. We agree that additional studies are needed to better characterize the correlation between tracer uptake and underlying metabolism. However, irrespectively of such correlation, differentiation of a PET volume from its background is an image segmentation issue that cannot be rigorously addressed using threshold-based methodologies. Those lead to inconsistent tumor volumes in most of the realistic clinical cases (1-5), especially heterogeneous ones (1,5,8). In these cases and in the absence of appropriate segmentation tools, it may be more accurate (although less reproducible) to rely on manual delineation rather than fixed threshold.

The use of inappropriate segmentation tools will lead to misleading conclusions regarding the potential of FDG PET in guiding radiotherapy treatment planning or as a prognostic and predictive factor for therapy response (9). As new algorithms become available and the clinical research applications demonstrate their potential, the medical equipment and software industry should implement them. Societies should develop minimum standards and guidelines regarding functional volumes segmentation, first in clinical research and eventually in clinical practice. This is a slow process and misleading conclusions as a result of the use of inappropriate approaches will reduce the interest of the technique, slowing even further the process of making available new technology. We therefore suggest a more radical stance with avoiding the use of

any fixed threshold based definition of PET metabolic tumor volumes in the future, especially if they are to be used for any PET image guided therapy application.

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